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ABSTRACT

Interest in physiology/cognition relations is increasing, in step with the realization that the individual ages as a whole, adaptive, living system. If a physiological system declines, a person's cognitive abilities may be reduced, unless some compensatory mechanism operates. Understanding this set of relationships permits potential interventions. This study explored the influences of blood pressure on memory for designs and Wechsler Adult Intelligence Scale vocabulary performance in terms of seven theoretical models which test not only for linear effects but for effects having a more complex, nonlinear time-lagged form as well. Each of a large number of hypotheses was tested twice, first with systolic, then with diastolic pressure variables. The 25-year data base of the Baltimore Longitudinal Study of Aging was used. Significant complex relationships between blood pressure and cognition were found. The theory that best fits results of this study is that optimal pressure delivers optimal oxygen to the brain, and optimal pressure depends on the state of the whole system, maintained and adjusted by age related feedback loops connected to both blood pressure and cognitive adaptive systems. The use of nonlinear, lagged multivariate models is recommended, since these hypotheses received support. (Author/ABL)

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Models of Physiology/Cognition Relations: Their Prevalence in the Literature and Their Utility in Examining the Effect of Blood Pressure on Vocabulary and Memory for Designs

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Abstract

Interest in physiology/cognition relations is increasing, in step with the realization that the individual ages as a whole, adaptive, living system. If a physiological system declines, a person's cognitive abilities may be reduced, unless some compensatory mechanism operates. Understanding this set of relationships permits potential interventions.

This paper explores the influences of blood pressure on memory for designs and WAIS vocabulary performance in terms of seven theoretical models which not only test for linear effects but for effects having a more complex, nonlinear time-lagged form as well. Each of a large number of hypotheses was tested twice, first with systolic, then with diastolic pressure variables. These studies are summarized in this brief paper under metamodel descriptions (e.g., "change influences change"). The 25-year data base of the Baltimore Longitudinal Study of Aging was used. Significant complex relationships between blood pressure and cognition were found. The use of nonlinear, lagged multivariate models is recommended, since these hypotheses received support.

Literature published mainly in the last thirty years indicates that there has been considerable interest in the relation between physiological variables and cognitive performance. This interest increases when aging is a factor under consideration. In any complex living system (Miller, 1978) one system (e.g., a cognitive one) is often influenced by another system (e.g., a physical one). This is important for older persons in particular since for them various physical systems often become less functional. If a physiological system declines, the person's cognitive abilities may also decline, unless some compensatory mechanism begins to function. It seems important, then, to gather all the information we can on the effects of physiological decline on cognitive performance so that we can better understand causes of cognitive decline (or improvement) with age. Understanding physiology/cognition relations also permits possible physiological interventions that could indirectly improve cognitive performance.

In this paper, then, we discuss the influence of physiological variables on cognition by specifically examining the effect of one such variable, blood pressure, on two cognitive variables, WAIS vocabulary performance and memory for designs (Benton Visual Retention Test). A large number of specific hypotheses were tested. In this paper these tests are summarized by means of several theoretical models, some of which describe effects having more than a simply linear form. This study also is rare in that it contains data from a twenty-five-year data base which permits effects with long lag times to become evident, if they exist.

Models used in the past

There have been a surprisingly large number of empirical physiology/cognition studies; 122 relevant reports have been published. Yet previous studies of this type used very few of the possible models by which we might relate physiological and cognitive performance. Various models might describe the relationships of interest in these studies.

Such models differ in terms of whether level or change are examined, whether effects are immediate or delayed, whether effects are linear or nonlinear, whether effects are reversible or irreversible, whether effects are cumulative or not, whether dynamic homeostasis is a factor, and whether other factors (such as health status) are included in that model.

First (Model 1), it is possible to have linear relationship between the level of a physiological variable at a certain time and the level of a cognitive variable at that time. For example, the higher one's blood pressure at a given time, the poorer one's memory for designs may be at that time. This is consistent with an immediate, reversible effect of physiology on cognition, one in which increments in variables are proportional. When pressure value increases, cognition decreases proportionally. Whatever the effect of blood pressure, the model assumes that if pressure was high and if pressure drops, the cognitive effect will not remain but will reverse to follow pressure. Only one time point is examined in such a model. As will be shown later, this model describes the majority of the physiology/cognition studies performed to date.

However, second (Model 2), it is also possible that not level but change is important, and that a change in physiology is linearly related to a change in

cognition. For example, blood pressure is measured at two times and memory for designs is measured at the same two times. The difference between Time 1 and Time 2 is calculated and used in analyses. This model is consistent with an immediate, reversible change effect in which increments are proportional, and in which cognitive changes alter direction when pressure changes alter direction. It also demands some form of a longitudinal study.

Third (Model 3), one can imagine a situation in which the level of a physiological variable at time one is related linearly to the change in a cognitive variable in the period between Time 1 and Time 2. For example, systolic pressure at time one may be proportionally related to the amount of decline in memory from Time 1 to Time 2. This is consistent with a long term irreversible cumulative effect, the amount of the change (absolute change or positive change or negative change, depending on the hypothesis) being linearly related to the level of the physiological variable.

Fourth (Model 4), it is possible that the amount of change (absolute change, positive change, or negative change, depending on the hypothesis) in the physiological variable between Time 1 and Time 2 is linearly related to the level of the cognitive variable at time 2. For example, perhaps persons with very labile pressures over a period of time gradually "wear down" the whole system so that with each increment in "wear and tear" comes a lower memory score at Time 2. This is consistent with a long term, irreversible, cumulative, proportional effect in which these "semi-lagged" correlations were high even if present-time correlations were not.

The fifth model (Model 5) (or set of models, in this case) is one in which in any of the previous models the effect is "lagged" in a greater degree

than in Model 3. In other words, expanding on the first model, the physiological variable level at Time 1 is linearly related to the cognitive variable level at a later time, Time 2. For example, a high blood pressure at age 20 may be related to a poor memory at age 30 and 40 (but not at age 20). This model adds the supposition that cumulative insult takes time to add up.

The sixth model (Model 6) (or set of models, in this case) contains nonlinear variants of each of the preceding models. It is possible (to extend model one) that some optimal level of a physiological variable exists that effects a cognitive variable level, one such that too much or too little has a negative effect but a moderate amount of that variable has a positive effect. It is also possible that a threshold exists such that once a certain level is reached, the effect is present, but not before (Birren's discontinuity hypothesis; Eisdorfer, 1977). An example of this latter sub-model is the idea that once one has had high blood pressure, permanent vascular damage and therefore permanent cognitive damage results.

Since blood pressure data were gathered more frequently than at Times 1,2,3, certain additional data points were involved in creating the nonlinear ("transformed") blood pressure change variables, and to avoid unnecessary complexity or confusion later they will be described here. A "transformed change #1" included all the changes calculated between sets of two consecutive data points from the time the respondent starts being tested until the usual Change 1 endpoint at Time 2 (Change 1= T2 minus T1; see Model 2). A "transformed change #2" included all the changes calculated between sets of two consecutive data points from the normal start of the Change 2 interval (i.e., Time 2) to the normal end of the Change 2 interval (i.e., Time 3) (Change 2 =

T3 minus T2: see Model 2). A "transformed change #3" included all the changes calculated between sets of two consecutive data points from the time the respondent starts being tested until the usual Change 3 endpoint at Time 3 (Change 3 = T3 minus T1: see Model 2). The reader may see on pages 15 and 16 that respondents with too few data points were not permitted to remain in the sample.

Finally, a seventh model (Model 7) (or set of models, in this case) supposes that some sort of dynamic regulation is occurring so that one variable compensates for or amplifies another in such a way that the system remains viable. Thus several joint effects must be considered. For example, memory may be negatively affected if systolic pressure is high in an <u>older</u> person who has <u>low</u> diastolic pressure <u>and</u> in a <u>younger</u> person who has <u>high</u> diastolic pressure. Thus, in any of the models above, joint effects might enter in and compensatory effects might wash each other out.

The models may therefore be regarded as theories. While specific <u>hypotheses</u> are tested, results also speak to <u>theory</u>. This distinction is an important one in a paper such as this where results of many hypotheses tests must be summarized very briefly under the banner of a model presenting the "big picture".

Published or presented empirical studies relating physiological variable(s) are summarized in Table 1. We attempted to be exhaustive, but did limit the review to studies of adult humans published in English language journals. Studies are categorized by the implicit model the researcher appeared to use. Information is given in the Table about respondents who were studied, variables used, and results. The final entries in the Table are for studies testing some form of the "terminal drop" hypothesis in which survivor status is the "physiological variable" in question, albeit a gross one. It is abundantly clear from the Table that the great majority of studies test Model 1. There is support for the hypothesis that physiology is related to cognition.

Insert Table 1 about here

Blood pressure effects

In this paper we are focusing on blood pressure effects in our tests of the models. For the studies in Table 1 involving blood pressure, the general hypothesis is that elevated blood pressure is associated with poorer cognitive performance.

The main accepted explanations for the hypothesized association are best expressed by Miller, Shapiro, King, Ginchereau, and Hosutt (1984); all depend on the mediation of the central nervous system (CNS). One accepted explanation is that elevated blood pressure may have detrimental effects on the central nervous system as it does on the heart and kidneys, and such CNS effects would be seen as a performance change. One effect of hypertension is a higher probability of cardiovascular disease (CVD). CVD is related to slower alpha rhythms in the EEG and increased delta, and therefore to potentially diminished creative/generative thought (Obrist and Bissell, 1955). A second potential explanation is that basic CNS changes are manifest in all systems including both the cardiovascular system and behavioral systems. Third and fourth potential explanations are that built in genetic factors or the passage of time itself bring about both cardiovascular disease and performance impairment. Additional potential explanations are based on the need for oxygen in all tissues including the brain, and suggest that some optimal pressure would lead to optimal delivery of oxygen and removal of waste products. Such optimal pressure would be modified by the state of the whole system, and would vary

based on health and context factors. For an older respondent with narrowing of blood vessels, then, higher pressure would be desirable, not detrimental, for good performance because it would mean that the system is getting what it needs to function. The system seems to be so sensitively regulated that even when persons face only a short term "difficult" task, or mental arousal, the system delivers a higher pressure (Contrada, Wright, and Glass, 1984; Conway, Boon, Jones, and Sleight, 1983). The alternative dynamic potential descriptions just described do not preclude feedback loops. Performance may influence physiology (in this case, blood pressure) just as physiology influences performance. The evidence in Table 1 studies can best be described as offering limited support for the hypothesis that blood pressure influences cognition.

Purpose of this study

In this paper we will describe results of testing the general hypothesis that blood pressure influences cognition, using the models described above. The key variables involved in these analyses are blood pressure, WAIS vocabulary, and Benton Visual Retention Test errors (BVRT) data from the Baltimore Longitudinal Study of Aging. This analysis supplements previous research by increasing the variety of relations examined and doing so in an extensive longitudinal data base.

Method

Subjects

Respondents were members of the Baltimore Longitudinal Study of Aging (BLSA). Characteristics of this subject pool are described in Shock et al.

(1984). Respondents were unpaid volunteers, generally of high socioeconomic status and white. Most of them resided in or near the Baltimore-Washington area; on the whole they were healthy, highly educated, and motivated. Only male respondents' data were used since females only recently were admitted to the program and therefore had too small and brief a data base. The male subject pool (i.e. men studied in the BLSA) included 1142 men between the ages of 17 and 96 (at last birthday) at the time of initial testing.

Some respondents in this pool were excluded from all analyses or from selected analyses. Only respondents with at least three data points over time (data recorded approximately every 6 years over approximately a 12-year period) on BVRT or WAIS and blood pressure recorded during the same visit, were included. Those blood pressure data points which were first-visit pressures (i.e., measures obtained during the respondent's first stay at the Center) were excluded due to observed "first-visit stress effects." Those blood pressure data points on which right-arm and left-arm pressures differed by two or more standard deviations from the mean of differences (obtained from a distribution of pressures of all Ss on all visits) were also discarded as atypical. This left a group of 290 respondents that will be termed the primary useable sample.

Some respondents in the primary useable sample were selected or excluded in later analyses based on age or health criteria. Health selections/exclusions focused on presence or absence of cardiovascular problems which would influence blood pressure and on use or non-use of blood pressure altering medications. This health screening was based on methods described in Wysowski, Andres, Tobin, Norris, and Shock (1981). In analyses reported below "All" subjects

refers to the primary useable sample, "Young" refers to a group age 20-39 at first data point, "Old" refers to a group age 60-79 at first data point. Respondents younger than 20 or older than 79 were excluded due to the potential effects of several outliers on smaller samples. Further, in analyses reported below, "Clean" refers to those respondents who were evaluated for the health criteria and who did not show cardiovascular problems and did not use pressure-altering medications.

Measures and Procedure

Three measures were central to these analyses: blood pressure, WAIS vocabulary, and memory for designs. Casual systolic and diastolic blood pressure was measured during the respondents general physical examination, given each visit, and before venipuncture or any other invasive procedure. Pressure was measured in both arms at the level of the brachial artery by physicians using mercury sphygmomanometers with standard-sized cuffs (14 cm x 52 cm). This took place on the morning of the first day of testing during each visit while participants were in a seated position. The right arm pressure was used for analyses. Right-left pressures were very highly correlated.

The first cognitive test, the WAIS vocabulary subtest (WAIS-V), is part of the Wechsler Adult Intelligence Scale (WAIS) and involves defining 40 words. The resulting raw score of 0-2 for each word reflects the respondent's understanding of the words. The second cognitive test, the Benton Visual Retention Test (BVRT) (Benton, 1963) is a nonverbal memory test made up of 10 designs each having one or more figures. The respondent inspects each design

for 10s and then reproduces it from memory. The measure is the total errors on all 10 designs. The WAIS-V and BVRT in various forms were administered individually during a single session, and were repeated approximately every 6 years.

Results

Plan of Analyses

The plans of analysis for blood pressure effects on BVRT and for blood pressure effects on WAIS-V were the same. The goal was to test the models described earlier, all in some way addressing the hypothesis that blood pressure is related to cognitive performance. In each case several specific hypotheses were tested.

The first step was to examine descriptive data for levels and changes in blood pressure, WAIS-V, and BVRT. Levels were described at each of the three time points; changes were described between each two time points. Times between Time 1 and Time 2 were always at least six years; times between Time 1 and Time 3 were at least 12 years; times between Time 2 and Time 3 could vary.

The second step was to test hypotheses subsumed by models, first using ANOVA and the entire primary useable sample. If blood pressure was related to cognition, ANCOVAs were calculated to remove the effects of age statistically. Step wise regression (MR) analyses with age entered first and blood pressure entered second as predictors were also carried out (and proved to be more sensitive than ANOVA) followed by ANOVA and MR on age/health subsamples drawn from the primary useable sample. All models were tested in this way for Time 1 data, Time 2 data, Time 3 data, changes T1-T2 data, changes T2-T3, and changes T1-T3 data.

Finally, if a hypothesized relationship between blood pressure and cognition was supported in one subgroup, attempts were made to replicate that finding in other subgroups or on other analyses in which it would also reasonably be expected to appear. In this way the large data base provided for replications and for rejection of chance findings. It was also possible with this data base to examine stability of individuals' scores. Analyses which offered statistically significant support ($p<.05$ or less) for a model are given in this paper. A lower alpha was not chosen since a lower alpha choice would preclude reporting multiple correlations with very large absolute values obtained in subsamples with a small N.

In the results reported below, blood pressure--when categorized for use as an independent variable in an ANOVA model--was grouped as follows: systolic-- $\geq$ 140, 130-139, 120-129, $\leq$ 119; diastolic-- $\geq$ 90, 80-89, $<$ 80. The upper cutoffs ($\geq$ 140 systolic, $\geq$ 90 diastolic) were chosen to conform with clinical diagnostic criteria and with descriptive analyses of the sample.

Study I

Relations Between Blood Pressure and BVRT

Analyses were first done with BVRT error scores, which have been shown to increase with age (Arenberg, 1978). Individuals demonstrated a considerable range of variation over time resulting in rather low stability coefficients. When T1, T2, T3 blood pressure levels were intercorrelated, the range of correlations

was (118 - 246) .40 to .58. When T1, T2, T3 BVRT errors levels were intercorrelated, the range of correlations was (279) .50 to .67. When changes in pressure T1-T2, T2-T3, were intercorrelated, the correlation was SYS(111) - .35 and DIA(219) - .46. When changes in BVRT errors T1-T2, T2-T3, were intercorrelated, the correlation was (279) -.40. Although scattered results were significant for each model, only Models 6/7 received strong support. So, only Model 6/7 (i.e. nonlinear effects examined in age/health subgroups) significant results will be reported in any detail (Table 2).

Test of Model 1: Level Effects Level. This model is based on the hypothesis that level of blood pressure is linearly related to level of BVRT errors at any one time. Analyses of covariance (ANCOVA) which controlled for age in assessing effects of blood pressure on BVRT, and MR analyses in which age was entered first, before blood pressure, with BVRT dependent were calculated at each of the three Time points. ANCOVAs and MRs for systolic pressure effects were nonsignificant at Time 1 and Time 3, but were statistically significant at Time 2. ANCOVAs and MRs for diastolic pressure effects were found to be minor and nonsignificant. Thus the first model was not supported to any extent. Since pressure at any Time was correlated highly and significantly with the highest pressure prior to that point (correlation range = .70 to .84), and since pressure at the Time point had no significant effect on performance, we decided prior pressure would not differ in its effects and therefore the "irreversible effects" form of Model 1 (i.e., the model that hypothesizes that effects linger, attenuating later correlations) was not worth testing.

Test of Model 2: Change Effects Change. This model is based on the hypothesis that a change in blood pressure will lead linearly to a change in BVRT errors. Change was calculated between all three pairs of Time points. Change 1 was equal to Time 2 measure minus Time 1 measure; change 2 was equal to Time 3 measure minus Time 2 measure; change 3 was equal to Time 3 measure minus Time 1 measure. Relations between pressure changes and simultaneous BVRT performance changes were not significant for either systolic or diastolic pressure.

Test of Models 3 & 4: Level Effects Change; Change Effects Level. The first of these two models tests the hypothesis that level of blood pressure influences the change in BVRT performance over the next time period. The second of these two model tests the hypothesis that a change in blood pressure influences the level of BVRT errors at the end of that change period. Analyses failed to demonstrate significant effects for either systolic or diastolic pressures, for either model.

Test of Model 5: Delayed Effects. This set of models tests hypotheses that effects in the first four models occur, but are delayed. In other words it tests whether an earlier pressure linearly effects a later test of performance. ANCOVAs and MRs were repeated, this time looking at Time 1 level effects on levels at Times 2 and 3, Time 2 level effects on Time 3 levels, change 1 effects on change 2, Time 1 level effects on changes 1, 2, and 3, and change 1 effects on Time 3 levels. Since only two significant effects were obtained in MR analyses, this model was rejected. In the delayed levels-effect-levels MR analyses, pressure did not add significantly to the R^2 for age.[1]

Test of Model 6: Nonlinear Effects; Cumulative Effects. This set of models tests the hypotheses that some optimal (or catastrophic) pressure exists that effects performance, or that some accumulated number of insults related to pressure are associated with effects on performance. This model has as an underlying assumption that damage caused by pressure is irreversible. Several different ways of conceptualizing this model were created by in some way weighting or selecting BP scores that reflected critical pressure or curvilinear effects("transforming" variables; see page 5). One was to relate highest prior pressure or positive change or mean pressure or change prior to cognitive performance, since the highest pressure or change the system ever had to bear might be a critical value. Another was to relate the mean of squared prior pressures or the square root of the mean of squared prior pressures to performance, to weight for the damage caused by earlier accumulated insults. A third was to relate the mean number of extreme ($\bar{X} \pm$ one sd) pressures to performance, to see if the frequency of insult to the system (as opposed to the degree of insult) is a factor in cognitive performance. A fourth was to relate the mean value of extreme pressures to performance. A fifth was to weight extreme prior pressures by making other than extreme pressures equal to zero or by doubling extreme pressures. These data manipulations were performed for systolic and for diastolic pressures. ANCOVA and MR analyses were performed, as usual. Simultaneous and delayed analyses were done, and both level and change scores were examined. Respondents from the primary useable sample who had fewer than 5 pressure data points prior to Time 2, or fewer than 8 pressure data points prior to Time 3 were eliminated from these analyses.

For diastolic pressure, mean number of negative diastolic changes up to and including Time 2 negatively related to the change in errors from Time 1 to Time 2. Model 6 therefore received some support, but it was too minimal to merit much attention.

Test of Model 7: Joint Effects and Compensatory Processes. This set of models tests hypotheses that systolic and diastolic pressure jointly influence performance, that pressure regulates itself by adjusting downward after an upswing or adjusting upward after a downturn to maintain a person's own usual level, and that additional variables like age or medication use have effects on the relations between pressure and performance. Earlier analyses were repeated, with modifications.

Joint effects were examined using two approaches: 1) entering the crossproduct of systolic and diastolic pressures into the MR equation after age, systolic alone, and diastolic alone; and, 2) examining selected subgroups which had specific patterns of high or low or changed systolic and diastolic pressures. (The latter were tested in old respondents only, and will be discussed below with the Old group results.) The crossproduct of systolic and diastolic scores was not found to contribute significantly to the MR equation after age, systolic and diastolic terms had been entered. In this first test (using all Ss, not subgroups) the joint effects hypothesis was not supported.

Additional variables of age and health status may modify the relationship between pressure and errors. (Certainly there are many more variables which also do so, but, for the time being, these two were chosen as most relevant.) The age variable had been addressed earlier by simply eliminating age statistically. (In spite of the restricted age range of age subgroups, age was still

frequently a significant predictor of BVRT errors). However, it is highly possible that in a dynamic adaptive system, the very nature of relations might be different for older or younger systems. So rather than eliminate age, it might make more sense to target age groups for more intense analyses. Consequently, analyses already mentioned were repeated for subsets of older (age 60-79) or younger (age 20-39) respondents. Health status/medication use descriptors were described earlier; these were used to group for "health status". "Clean" indicated that the respondent did not show cardiovascular symptoms or use pressure altering medications. So, significant analyses will now be reported and contrasted for the All Clean subsample (N = approximately 142), the Old subsample (N = approximately 51), the Old Clean subsample (N = approximately 28), the Young subsample, (N = approximately 55), and the Young Clean subsample (N = approximately 32).

The delayed effects model (Model 5) was examined again for the five subsamples. Model 5 received some very minimal contradictory results, and therefore the model was not supported.

Transformed data were analyzed for subgroups in this Model 7 re-analysis of Model 6. A large number of significant results were found. Significant results are in Table 2.

Insert Table 2 here

For the <u>All Clean</u> group, there were several significant effects. The mean number of positive diastolic changesup to and including Time 2, positively related to error change from Time 1 to Time 2. The mean number of very negative

diastolic changes (1 sd or less from $\bar{X}$ of changes) up to and including Time 2, negatively related to error at both Time 2 and Time 3. The number of positive diastolic changes up to and including Time 2 related positively to error change from Time 1 to Time 2; the opposite was true for negative changes in pressure. The mean number of very positive systolic changes (i.e. 1 sd or more from the $\bar{X}$ of changes) up to and including Time 2 negatively related to change in errors from Time 2 to Time 3. Mean systolic change up to and including Time 2, when large positive changes were weighted, negatively related to error change from Time 2 to Time 3. The mean systolic change, and the mean number of positive changes, or the mean change with negative changes weighted, from Time 2 to Time 3 negatively related to error change from Time 2 to Time 3.

For the Old subgroup there were several significant effects. The square root of mean squared diastolic changes up to and including Time 2 negatively related to error at Time 2. The highest diastolic change Time 2 to Time 3, negatively related to error at Time 3. The highest diastolic change up to and including Time 2, negatively related to the change in errors from Time 1 to Time 2. The highest systolic change from Time 2 to Time 3 negatively related to error level at Time 3. Mean systolic change, mean number of positive changes, and the mean change with positive changes weighted, from Time 2 to Time 3 negatively related to error at Time 3. The mean number of negative systolic changes from Time 2 to Time 3 positively related to error at Time 3. The mean number of positive systolic changes up to and including Time 3 negatively related to error at Time 3. The mean number of negative systolic changes up to and including Time 2 negatively related to the error change from Time 1 to Time 3. For the Old Clean subgroup there were several significant effects. The mean number of

very positive diastolic changes up to and including Time 2 negatively related to error at Time 3. Mean systolic change up to and including Time 3, and the mean number of positive changes, negatively related to error at Time 3. Mean systolic change and the mean number of positive changes from Time 2 to Time 3 negatively related to error change, Time 2 to Time 3. Mean systolic change up to and including Time 2 positively related to error change from Time 1 to Time 3. The mean number of negative systolic changes up to and including Time 2 negatively related to error change Time 1 to Time 3. The mean very negative systolic change up to and including Time 2 positively related to error Time 1 to Time 3. Mean systolic change up to and including Time 3 negatively related to error change Time 1 to Time 3. For the Young subgroup there were several significant effects. The highest diastolic change up to and including Time 2 positively related to error change from Time 1 to Time 2 and from Time 1 to Time 3. Mean systolic very negative weighted change from Time 2 to Time 3, negatively related to error level at Time 3. Mean systolic change, very negative changes weighted, up to and including Time 2 positively related to error change from Time 2 to Time 3. The mean number of negative systolic changes up to and including Time 3 positively related to error change from Time 1 to Time 3. The mean number of very negative systolic changes up to and including Time 2, negatively related to change in error from Time 2 to Time 3, and positively related to change in error from Time 1 to Time 2. For the Young Clean subgroup there were several significant effects. Mean squared diastolic change as well as the square root of those means, up to and including Time 2, negatively related to error at Time 2. The mean squared diastolic change, as well as mean square root, up to and including Time 2, positively related to change in error from Time 2 to Time 3.

The mean number of very negative diastolic changes up to and including Time 2, also positively related to change in error from Time 2 to Time 3, and related to fewer errors at Time 2. The mean systolic change, weighted for very positive changes, up to and including Time 2 negatively related to error change Time 2 to Time 3.

Joint systolic/diastolic effects were studied in the Old subgroup using two additional strategies. These included labeling sub-subgroups as to whether, from Time 2 to Time 3: (1) systolic rose from some lower figure to $\geq$ 140 ("high") and diastolic did not go up; (2) systolic was high and level while diastolic was high ($\geq$ 90) and level; (3) systolic stayed high while diastolic rose to $\geq$ 90; or 4) systolic and diastolic both rose. Groups did not differ significantly in errors, but the first two groups increased in errors while the last two stayed the same. N's were very small. In another approach to this problem, systolic pressure was held constant ($\geq$ 140) from Time 2 to Time 3 and those high systolic respondents were further grouped as low diastolic (< 80) or high diastolic (> 90). Results were not significant.

On the whole there was support for Model 7. Age groups and health groups appeared to have different dynamics. To simplify results greatly, for the Old and Old Clean, with age controlled, systolic or diastolic rise or change (flexibility) was related to better performance. For the Young with age controlled, systolic rise was associated with more errors. For the Young Clean, though, a diastolic rise or change at a given time was associated with better performance at that same time, but poor performance at a later time. For the All Clean, systolic pressure rises helped and diastolic rises hurt performance.

Summary: Blood Pressure and BVRT Errors

There was support for the general hypothesis that pressure is related to BVRT errors. Most of this support came from Model 7 tests of specific hypotheses described by analyses which suggested that systolic or diastolic blood pressure rise and the system's ability to fluctuate aid short and longer term performance in the old, but are less clearly valuable for the young.

Study II

Relations Between Blood Pressure and WAIS-V

MR analyses were repeated for WAIS vocabulary, which has been shown to be stable with age (Arenberg, 1978). Results are in Table 3. In these MR analyses, age was entered first and the blood pressure variable was entered second to predict WAIS-V.

Insert Table 3 about here

Test of Model 1: Level Effects Level. This model is based on the hypothesis that pressure is linearly related to scores at any time. In the MR analyses, systolic and diastolic pressure contributed significantly to the equation predicting WAIS-V Time 1, the former having a negative weight and the latter having a positive weight. So Model 1 received some support. The higher the systolic pressure and the lower the diastolic pressures at Time 1, the lower the WAIS-V score.

Test of Model 2: Change Effects Change. This model tests the hypothesis that change in pressure linearly effects change in vocabulary over the same time period. There was no significant linear effect of pressure change on vocabulary

change for the primary useable sample. This model was not supported.

Test of Models 3 and 4: Level Effects Change; Change Effects Level. This test first addresses the hypothesis that level of pressure influences change in vocabulary scores over the next time interval. It then tests the hypothesis that change in pressure over two time points influences vocabulary scores at the second time point. Neither hypothesis was supported for the primary useable sample.

Test of Model 5: Delayed Effects. This set of models tests hypotheses that effects in the first four models occur, but are delayed, so that an earlier pressure linearly effects a later vocabulary score. The model received no support in the primary useable sample.

Test of Model 6: Nonlinear Effects; Cumulative Effects. This set of models hypothesizes that some optimal (or catastrophic) pressure exists that influences performance, or that some accumulated number of insults are associated with effects on pressure.

In general, transformed level variables were not related to vocabulary scores, but transformed change variables were. The following relations to WAIS-V levels were found. For diastolic pressure there were six significant effects. The number of positive changes up to and including Time 2 negatively related to vocabulary at Time 3. The mean change from Time 2 to Time 3 positively related to vocabulary at Time 3. The mean number of negative changes from Time 2 to Time 3, negatively related to Time 3 vocabulary. The mean number of very negative changes from Time 2 to Time 3, negatively related to Time 3 vocabulary. And the mean change--weighted in two different ways to accentuate very

negative changes--from Time 2 to Time 3 positively related to Time 3 vocabulary. For systolic pressure, the number of negative changes from Time 2 to Time 3 negatively related to vocabulary at Time 3. Model 6 therefore received some support. Multiple fluctuation in pressure seemed to be associated with lower vocabulary scores. The following relations to WAIS-V changes were found. The highest systolic change from Time 2 to Time 3, the root of squared systolic changes during that period, the mean number of very positive systolic changes during that period, and the mean systolic change weighted for high systolic positive changes during that period all negatively related to WAIS-V change during that period. The mean number of very low diastolic changes, up to and including Time 3 negatively related to WAIS-V change from Time 2 to Time 3 (and from Time 1 to Time 3). The mean very low change during that time positively related to both WAIS-V changes. Pressure drops seem related to WAIS-V increases.

Test of Model 7: Joint Effects and Compensatory Processes. This set of models addresses the hypotheses that systolic and diastolic pressures jointly influence performance, that pressure autoregulates, and that additional variables like age or medication use have effects on the relation between pressure and performance. Joint effects, where operationalized as crossproducts, were nonsignificant. Additional variables of age and health status/medication use were used, as before, to form All Clean, Old, Old Clean, Young, and Young Clean subgroups. Then previous model analyses were repeated. Significant results appear below, and in Table 3.

Concerning Model 1 (levels) in the Young Clean sample, both diastolic and systolic pressures at Time 3 significantly predicted vocabulary score at Time 3

and were negatively related to it.

Concerning Model 2 (change scores), for the Old group, and even more so for the Old Clean group, the change in systolic pressure from Time 1 to Time 3 was positively related to the change in vocabulary scores from Time 1 to Time 3.

Concerning Models 3 and 4 (level/change and change/level), for the All Clean group, the change in systolic pressure from Time 1 to Time 3 was positively related to vocabulary scores at Time 3. Level never significantly, reliably predicted change.

Concerning Model 5 (delayed effects), for the Young Clean group, systolic pressure change from Time 1 to Time 2 was positively related to vocabulary at Time 3; systolic change from Time 2 to Time 3 was negatively related to vocabulary at Time 3. For the Old, systolic change from Time 1 to Time 2 negatively influenced vocabulary at Time 3 and diastolic change from Time 1 to Time 2 positively influenced vocabulary at Time 3. For the Young Clean group, diastolic at Time 1 negatively influenced vocabulary at Time 3.

For Model 6 (nonlinear effects), there were a large number of significant findings for transformed change variables but none for transformed levels variables. Each entry may represent several analyses which agree with each other. For the All Clean group there were many significant blood pressure effects (systolic and diastolic). All of the following negatively related to vocabulary level at Time 3: mean diastolic change up to and including Time 2; mean number of positive diastolic changes up to and including Time 2; mean very negative diastolic change (doubled) from Time 1 to Time 2; and mean number of positive changes in diastolic up to and including Time 3. Mean number of very negative diastolic changes up to and including Time 3 negatively related to

vocabulary change from Time 2 to Time 3 and Time 1 to Time 3. The following related to the change in vocabulary from Time 1 to Time 2: the mean number of negative systolic changes, up to and including Time 2, negatively related. All of the following systolic variables related negatively to vocabulary change from Time 2 to Time 3: the highest change, from Time 2 to Time 3; the mean squared change, from Time 2 to Time 3; the root of squared change from Time 2 to Time 3; the mean number of very positive changes, from Time 2 to Time 3; the mean change (positive changes weighted), from Time 2 to Time 3; the highest change, up to and including Time 3; and the root of squared change, up to and including Time 3. The following variables related to change in vocabulary from Time 1 to Time 3: mean number of negative systolic changes up to and including Time 2 related negatively. For the Old group there were many significant blood pressure effects (systolic and diastolic). All of the following related to vocabulary level at Time 3: the highest diastolic change, the mean very negative diastolic change, the mean diastolic change, and the mean very positive diastolic change, from Time 2 to Time 3 positively related; the mean number of negative diastolic changes from Time 2 to Time 3 negatively related. The following changes were related to vocabulary change from Time 2 to Time 3: the mean square diastolic change (and its root) up to and including Time 2 negatively related. The following diastolic changes related to vocabulary change from Time 1 to Time 3: the highest change, up to and including Time 2, and the mean change with positive changes weighted up to and including Time 2 negatively related; the mean number of positive changes up to and including Time 3 positively related. The following systolic changes related to vocabulary change from Time 1 to Time 3: mean number of positive systolic changes from Time 2 to Time 3

positively related to vocabulary level at Time 3; the mean change (with negative changes weighted) up to and including Time 3 positively related. The mean number of systolic positive changes from Time 2 to Time 3 or up to and including Time 3 positively related to vocabulary change from Time 2 to Time 3. For the Old Clean group there were many significant blood pressure effects (systolic and diastolic). The following diastolic changes related negatively to vocabulary change from Time 1 to Time 3: the highest change up to and including Time 2; the mean change up to and including Time 2, with positive changes weighted. The following systolic changes related to vocabulary change from Time 1 to Time 2: the highest change, the root square change, and mean number of very negative changes, all up to and including Time 2, negatively related. The mean systolic change (with very negative changes weighted), up to and including Time 2 positively related to vocabulary change from Time 1 to Time 2. The following systolic changes related to vocabulary change from Time 2 to Time 3: mean number of positive changes from Time 2 to Time 3 or up to and including Time 3, positively related; mean number of negative changes from Time 2 to Time 3 negatively related. The following systolic changes related to the vocabulary change from Time 1 to Time 3: mean change (very positive changes weighted) up to and including Time 3 negatively related; the root mean square change, up to and including Time 2 negatively related; root mean square change, up to and including Time 3 negatively related; and mean change (very negative changes weighted) up to and including Time 3 positively related. For the Young group, only one systolic pressure variable was significant and related negatively to vocabulary at Time 3: mean square change from Time 2 to Time 3. For the Young

Clean group, the following diastolic changes related negatively to vocabulary at Time 3: mean number of positive changes up to and including Time 2; mean change up to and including Time 3; mean very negative change weighted, up to and including Time 3. The following diastolic changes related to change in vocabulary from Time 1 to Time 2: highest change up to and including Time 2, related positively; mean number of negative changes up to and including Time 2, related negatively. The following systolic changes related negatively to vocabulary at Time 3: mean change, mean number of positive changes, mean change weighting for very positive changes, all from Time 2 to Time 3; mean number of positive changes, up to and including Time 3.

Joint systolic/diastolic effects were studied in the Old subgroup using the additional strategies described earlier. When systolic pressure was high ($\geq$ 140), the mean vocabulary score (Time 3) of those with low diastolic pressure ($\leq$ 80 Time 3) was 54.0, with moderate diastolic pressure (80-89 Time 3) was 61.0, and with high diastolic pressure ($\geq$ 90 Time 3) was 68.5 [F (2,23) = 4.08, p .03]. This supported the hypothesis that if systolic was high, it helped performance to have a high diastolic.

Model 7 was supported since there were differential effects in age and health subgroups. There were fewer effects for young compared to old subjects. There were more effects in "clean" subgroups. For the All Clean group, the Old Clean, and the Young Clean group change or heightened pressure was detrimental to performance. For the Old group it seemed to aid performance.

Summary: Blood Pressure and WAIS Vocabulary

There was some support from tests of specific hypotheses for the general hypothesis that blood pressure is

related to vocabulary scores. Most of the support came from Model 6 and 7 analyses which suggested that for the old pressure increases are consistent with good performance, but for the young with no cardiovascular problems and no use of antihypertensives, pressure increases are not consistent with good performance.

Discussion

The primary purpose of this study was to examine several models of relations between blood pressure and cognitive performance to determine if any model describes that relationship. Results of tests of specific hypotheses demonstrated some support for the general hypothesis that pressure relates to cognition, irrespective of age. Primarily, such support comes from Models 6 and 7, for both vocabulary and memory for designs, although there is some minimal support for other Models. Pressure rise and system changibility seemed related to better BVRT performance for the old, but were of less clear benefit for the young. Pressure effects remained when age effects on BVRT were removed statistically for members of either old or young groups who were without cardiovascular diagnoses or antihypertensive medications. Pressure rise was related to better vocabularly performance for the old and to poorer performance for the young groups.

For the Old tested with the BVRT, the sheer number of previous changes in pressure seemed important, as did the absolute size and direction of those changes. The average amount of earlier change, as well as having a large earlier jump in pressure, were important. For the Young tested with BVRT, degree of earlier pressure change mattered, whether that degree of change was measured in number of rises or absolute value of highest previous pressure, or extent of positive or negative changes in earlier pressure. For the Old and the Old Clean tested with WAIS-V, highest earlier pressure, number of rises, number of earlier positive or negative changes, and earlier pressure change by almost any measure turned out to be largely beneficial in terms of performance. For the Young Clean tested with WAIS-V, number of earlier changes, magnitude of

earlier changes, largest earlier change--all were useful for predicting negative performance outcomes.

The best explanation for these events seems to be that the effects of blood pressure rises and fluctuations are cumulative and irreversible and sometimes delayed, irrespective of age, but that different age groups have different patterns of cognitive response to this. A reactive system may be a sign of health and be useful for cognitive performance, for the Old group though not for the Young. It may be that when a vascular system looses its ability to make many upward and downward adjustments, it mediates lower scores for older male respondents; or it may be that male respondents who are not motivated by the cognitive task and who do poorly are also the persons who are not moved by whatever events cause pressure reactivity in our other respondents, hence the correlation. Experimental studies could answer this question, and are planned. Studies with female respondents would indicate whether these phenomena are sex specific.

The hint in the data that higher pressure is "useful" for the old to do better on WAIS-V and BVRT raises questions. Perhaps the clinical definition of pathological pressure could be made age specific without increasing the risk of medical problems. Perhaps the price of antihypertensives, even if they are clinically indicated, is poorer cognitive performance, in older users, not because antihypertensives are designed to be psychotropic drugs, but precisely because they <u>are</u> effective in lowering blood pressure.

It was interesting to see that some significant effects of blood pressure are present across age groups, medication groups, and across both the cognitive tasks that are age-influenced and those that are age independent, even when

age effects were statistically removed. Yet in spite of the presence of significant effects across several samples, times and tasks, the data suggest that blood pressure may have differential significant age related effects because it is operating as part of a self-regulating system. For the Old, a WAIS-V score at a given time was positively related to prior pressures and future pressure rises, but negatively related to the future number of pressure changes. The person may experience cumulative, irreversible effects of high pressure that contain the seeds of their own continuation and acceleration. These "circular" effects, if they exist, are, for some reason, more apparent in the Old than in the Young and on vocabulary scores rather than on visual memory scores.

These results suggest that some interesting relationships may be overlooked in studies of physiology and cognition because the more complex models of the process are virtually never examined. If these data do indicate "slow-acting" blood pressure effects, medical interventions need to be more sophisticated, longer-term, and tailored to the cognitive and physical requirement and history of the patient.

Theories of the nature of possible mechanisms of blood pressure-cognition relations were described earlier in this paper. Given these data just reported, it would be hard to argue that such relations are due to general damage to the CNS. Most of the theories cited above also assume that any degree of old-age high blood pressure indicates disease, without considering the possibility some lesser rise in pressure may be a normal correction for a changing physical system.

The previously mentioned theory that best fits the data reported in this paper is

that optimal pressure delivers optimal oxygen to the brain, and optimal pressure depends on the state of the whole system, maintained and adjusted by age related feedback loops connected to both blood pressure and cognitive adaptive systems.

[1] If, however, the order of entry was reversed and systolic pressure values were entered first, pressure reduced the R^2 for age by half.

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Table 1

Studies Relating Physiology to Cognition, Categorized by Model

Study	Respondents	Variable or Materials	Significant Results
Model 1: Physiological Level Affects Cognitive Level at a Single Time			
1. BARRETT, WATKINS (1986)	N1=80; 60-75 N2=40; 18-33 men and women with and without cardiovascular disease	Cardiovascular status, unfamiliar word lists unfamiliar word lists	Those without cardiovascular disease performed better than those with it in free recall following semantic processing.
2. BIRREN, BUTLER, GREENHOUSE, SOKOLOFF, YARROW (1963)	47 men, 65-91	Cerebral metabolic rate, vital capacity	Multiple findings which will not be summarized here.
3. BIRREN, SPIETH (1962)	161 men, 23-60	Cardiovascular status, exercise, response speed, blood pressure	Pressure was not related to psychomotor speed.
4. BOLLER, VRTUNSKI, MACK, YOUNGJAI (1977)	40 men, mean age = 50 hypertensives and normals	Blood pressure, response time, IQ, digit span, visuospatial, logical memory	Hypertensives did worse on response time, IQ, digit span.
5. BOTWINICK, STORANDT (1974)	N = 96, men and women, 20-74	Cardiovascular status (self-report), auditory reaction time	In high education subjects, cardiovascular problem subjects were slower.
6. COHEN, EISDORFER (1977)	14 men, 23 women, 64-79	Immunoglobulin level, WAIS vocabulary, digit symbol substitution	No relation for women; for men, IgG positively related to vocabulary and digit symbol and IgA negatively related to vocabulary.

(table 1 continues)

7.	COHEN, EISDORFER (1980)	15 men, 42 women, 62-100 impaired 26 men, 39 women, 64-93; non-impaired matched for age & sex	Immunoglobulin levels, cognitive impairment (by clinical assessment)	The impaired had significantly higher IgG and IgA.
8.	COHEN, MATSUYAMA, JARVIK (1976)	5 men and 9 women, 83-100 years	Immunoglobulin levels, Terman vocabulary	Positive relation exists between IgM & IgG immunoglobulin levels and vocabulary scores.
9.	COSTA, SHOCK (1980) *see other models	350 men, 20-39, 40-49, 50-65, 66-84	Basal blood pressure, casual blood pressure, Army Alpha (timed and untimed)	The high pressure group performed least well on following directions, number series, arithmetic problems, synonyms/ antonyms, number series, practical judgement, and total.
10.	DORNBUSH, VOLAVKA (1976)	4 women, 2 men, mean age = 65.6	Peptide hormone ACTH(4-10), short term memory, perceptual speed, motor speed	Hormone administration improved attention and therefore response time in a dose-related way.
11.	EISDORFER (1968)	48 men 20-48 and $\geq$ 60	Free fatty acid in plasma, WAIS vocabulary, verbal learning	
12.	EISDORFER, NOWLIN, WILKIE (1970)	28 men, 60-78	Inderol administered to block arousal, WAIS vocabulary, digit span, Figure Embedment Scale, serial learning of high association words	Arousal blocking improved learning.
13.	ELIAS, ROBBINS, SCHULTZ, STREETEN (1986)	men and women I. 52 normotensives 43 hypertensives II. 10 normotensives, medicated	Hypertensive/normotensive status, Halstead-Reitan	The mean performance level of hypertensives was lower at both times I and II.

14.	ELIAS, ROBBINS, SCHULTZ, STREETEN (1987)	23 men, 31 women in each of 2 groups	Hypertensive/normotensive status, Average Impairment Rating Test	Hypertensives scored similar to normotensives.
15.	EL NAGGER (1982)	48 men, 24-68; 30 exercise, 18 don't	Exercise, "cognitive processing"	Exercisers perform better.
16.	ELSAYED, ISMAIL, YOUNG (1980)	70 men, 24-68	Blood pressure, heart rate, VO_2, fluid and crystallized intelligence	The highly fit scored higher on fluid intelligence, as did the young.
17.	ENZER, SIMONSON, BLANKSTEIN (1942)	No information	Diagnosis of circulatory insufficiency, critical critical flicker fusion frequency	CFFF was lower for those with circulatory insufficiency.
18.	FAITH, SÍPOS (1975)	11 Ss	Mountaineer status, climbing a mountain, memory for forty words	Mountaineers did better before climb; after climb, status made no difference.
19.	FRANCESCI, TANCREDI, SMIRNE, MERCINELLI, CANAL (1982)	7 men, 8 women, 39± 7 yrs.; normotensives 10 men, 7 women, 35± 9 yrs.; untreated hypertensives 13 men, 9 women, 43± 6 yrs.; treated hypertensives	Hypertension status, card sort, Wechler Memory Scale, Raven, Benton, W-B subtests (block design, picture assembly, digit symbol)	Both hypertensive groups groups did worse on card sort, Memory Scale, Raven, Benton, block design; the treated group did worse on picture assembly; no difference found on digit symbol.
20.	GOLDMAN, KLEINMAN, SNOW, BIDUS, KOROL (1974)	14 men, mean age 47.6 VA outpatients	Diastolic blood pressure, Category Test (Reitan)	Diastolic hypertension was related to errors on Category Test.
21.	GOLDMAN, et al (1975)	men, 35-68; 7 hypertensives 7 normotensives	Blood pressure, Category Test (Reitan)	Pressure was related to errors on the Category Tests.

22. HAGBERG (1978)	13 men, 54.1± 4.5 yrs. 3 women, 62.0± 3.5 yrs.; 16 organic dement	Blood flow in left hemisphere brain regions, verbal memory, memory for designs & objects	Blood flow was related to performance on tasks.
23. HERZOG, SCHAIE, GRIBBIN (1978)	75 men, 81 women; many different cohorts from ongoing study	Cardiovascular disease, hypertensive status groups, PMA subtests, Test of Behavioral Rigidity	At each of two times, cardiovascular disease group did more poorly on all cognitive variables except one subtest. Hypertension plus antherosclerosis group did more poorly on number, word fluency, intellectual ability, educational ability subtests. Hypertension only group did more poorly on intellectual ability.
24. JACOBS, WINTER, ALVIS, SMALL (1969)	18 men mean age 68	Breathing pure oxygen, Wechler Memory Scale, Bender-Gestalt, Tien's Organic Integrity Test	Those breathing pure oxygen had better test scores.
25. JALAVISTO (1964)	130 women, 40-93	Blood pressure, retinal rivalry, vital capacity, memory for pictures, memory for number --reverse digit span.	Retinal rivalry was related to all the other variables except blood pressure.
26. JALAVISTO (1964-65)	86 women, 40-93	Vital lung capacity, maximum capacity, critical flicker fusion, reaction time, tapping rate, memory for pictures, memory for backward digits, blood pressure.	Systolic and diastolic pressures are positively correlated with reaction time and negatively correlated with memory. Lung function is positively correlated with reaction time and memory.

27.	KARASAWA, KAWASHIMA, KASAHARA (1979)	20 men, 95 women ≥ 100 years old 49 men, 49 women 90-99 years old	Activity level, blood pressure, sensory processing	Physical functioning was related to mental funtion. Higher systolic pressure related to better performance.
28.	KEDZI, ZAKS, COSTELLO, BOSHES (1965)	120+ cardiac patients	Cardiac status, neurological function, IQ, digit symbol substitution, Bender Gestalt, perceptual tests	4% of cardiac patients have some neurological dysfunction; congestive heart failure patients have lower IQ, poorer digit symbol.
29.	KING (1956)	22 male schizophrenics	Hyper- and hypotension (defined as the extreme pressures in this group), reaction time, tapping speeds	Hypertensives give slower responses (but potential medication effects).
30.	KLEBAN, GRANICK (c. 1976)	47 men, 65-91 (Ss used in Birren & Butler, et al, 1963)	Blood pressure and blood flow variables, cerebral oxygen consumption, glucose consumption, WAIS, perceptual/verbal tests, reaction time	Pressure was negatively related to performance variables other than reaction time.
31.	KLEE (1964)	men, 34-61; 11 patients	Clinically evaluated mental deterioration, cerebral metabolic oxygen consumption.	Deterioration was related to lower CMRO2.
32.	KLEINMAN, GOLDMAN, SNOW, KOROL (1977)	8 men, 26-63; essential hypertensives	Blood pressure, category test of Halsted-Reitan	Errors on category test were related to pressure.
33.	KRASNO, IVY (1950)	(several studies reported) (usually patients)	Hypertensive status, CFF threshold	CFF was lower in patients with hypertension or anemia and improved with therapy.

34.	LASSEN, MUNCK, TOTTEY (1957)	17 men, 2 women, 26-67; 19 hospitalized patients: 6 normal with high blood pressure, 3 demented with high blood pressure, 10 demented unclassified	Cerebral metabolic oxygen rate, blood pressure, block pattern test, digit learning	CMRO had a linear relation to pattern test performance and curvilinear relation to digit learning.
35.	LICHTMAN, POSER (1983)	28 males, 36 females age 16-54	Exercise class vs hobby group, Stroop Color Word Test	Exercise group performed better on Stroop Test.
36.	LIGHT (1975)	203 men and women, 18-59	Blood pressure, response time	Medicated hypertensives were slower than the other hypertensives or the normotensives.
37.	LIGHT (1976)	18-77, N = 400+	Blood pressure, response time, short term memory, long term memory, Wechsler Memory Scale, recency recall, Wisconsin Card Sort Test	Hypertensives showed memory deficits; response time increased for treated hypertensives.
38.	LIGHT (1978)	271 men and women, 18-77	Blood pressure, serial reaction time	Treated hypertensives had a longer reaction time.
39.	MANTON, SIEGLER, WOODBURY (1986)	Duke Longitudinal study participants, N = 267, age 60+ at first test period men and women	Diastolic pressure, general physical health, WAIS, Wechsler Memory Scale, response time	Self-rated health was related to cognitive functioning. High pressure was usually related to poor performance, except in a few cases when it was related to very good performance.
40.	MANUCK, CORSE, WINKELMAN (1979)	45 men, 25-62	Blood pressure, concept tasks	Pressure reactors did not differ from nonreactors in performance on conceptualization tasks.

41.	McGLYNN, LAUGHLIN , ROWE (1979)	15 women, 18-23	Exercise at various speeds, line matching	Speed status did not effect line matching.
42.	OBRIST (1963a)	28 male undergrads	Blood pressure, heart rate, respiration, concept problems	Accuracy and speed of perception was influenced positively by experimental increase of heart rate.
43.	OBRIST (1963b)	47 males	Circulatory status, EEG changes, cognitive test battery	Circulatory status appeared to influence EEG, and thereby cognition.
44.	OBRIST, BUSSE, EISDORFER,	397 Ss, 60+	EEG, intelligence	No relation was found.
45.	OHLSSON, SJÖBERG, DORNIC (1975)	48 male students, 20-38	Prior fitness, bicycle ergometer, multiplication problems	Prior fitness reduced the effect of exercise on performance.
46.	PENTZ, ELIAS, WOOD, SHULTZ, DINEEN (1979)	15 men, 10 women; hypertensives 8 men, 8 women; examined normotensives 9 men, 12 women; general population normotensives mean age 26.3-50.8	Blood pressure, tactual performance, finger tapping, Category Test, WAIS	Hypertensives who were young differed more from normotensives who were young than their old counterparts differed from each other on tactual and tapping tests.
47.	PERLMUTER, HAKAMI, HODGSON-HARRINGTON, GINSBERG, KATZ, SINGER, NATHAN (1984)	178 men and women 55-74; diabetics - 46% women, control - 57% women	Diabetes status, digit span, serial learning	Diabetics had poorer performance.
48.	POWELL, EISDORFER, BOGDENOFF (1964)	48 men, 20-48 and 60	Plasma free fatty acids, learning 8 words	Older respondents had higher fatty acid level before, during, after learning.

49.	RICHTER-HEINRICH (1970)	30 normotensives 40 essential hypertensives 30 hypertentives 20% women ages 18-40	Blood pressure, mental arithmetic, sentence completion	Hypertensives made more errors.
50.	ROBERTSON-TCHABO, ARENBERG, TOBIN, PLOTZ (1986)	52 men, 33.0-86.7; noninsulin dependent diabetic, matched controls, 610 controls	Diabetic status, visual memory, WAIS vocabulary	Diabetes had no effect on cognitive status.
51.	ROSEMAN, BUCKLEY (1975)	Terminal elderly patients I. 70-94, 97 = N II. 46-71, 468 = N	Serum IgG, WAIS	There was an inverse relationship between serum IgG and intelligence.
52.	SANDS (1978)	120 women, ages 65-92	Blood pressure, WAIS	High pressure was related to decline in fluid abilities.
53.	SCHENK, LANG, ANLAUF (1981)	9 men, 4 women, mean age 38.8	Administration of beta-blocking antihypertensives, reaction time, concentration	Drugs improved concentration, reaction time.
54.	SCHULTZ, DINEEN, ELIAS PENTZ, WOOD (1979)	68 men or women, 45-65 or 21-39; hypertensives, plus 42 normals	Blood pressure, administration of diuretic, plasma renin, WAIS	Hypertensives were worse on the WAIS, young hypertensives doing worse than old. Given matched WAIS-V young showed greater BP effects than old on WAIS-P.
55.	SHAPIRO, MILLER, KING, GINCHEREAU, FITZGIBBON (1982)	48 men, 34 women, men, 33.7 hypertensive, 33.8 normotensive; women, 29.8 hypertensive, 29.4 normotensive	Blood pressure, visual recognition threshold, perception of spaced stimuli, critical fusion flicker, digit symbol substitution, block design, memory for designs, time judgement, psychomotor tests	Hypertensives did more poorly on visual recognition (women), digit symbol, time (women), and psychomotor tests.

56. SHVARTZ, MEROZ, MECHTINGER, BIRNFELD (1976)	6 men	Exercise, heat exposure, response to visual stimulus	Exercise was associated with increased response time.
57. SIEGLER (1983)	I. 127 men, 140 women, 59-94 II. 261 men, 241 women, 46-70	Cardiovascular disease status, IgG, blood pressure, WAIS	WAIS scores were higher for those without CVD; IgG levels related to health. Those with high blood pressure did better intellectually.
58. SJÖBERG (1975)	25 men, 21-34	Bicycle ergometer, reaction speed	Reaction time in visual choices had an inverse U-shaped relationship to work load on the bicycle ergometer.
59. SJÖBERG (1980)	48 men, mean age 24	Fitness status, physical work, paired associate learning, rapid mental arithmetic	After physical work, the more fit performed better than the less fit.
60. SPIETH (1964)	men 35-59; N = 475	Blood pressure, cardiovascular status, Trailmaking test, stimulus matching serial reaction time test, Halstead Tactual Performance Test, digit-symbol substitution, block design	On speeded tests, medicated hypertensives and the healthy were faster. On the Halstead, the healthy were faster than most other groups. On block designs, selected CVD or pressure groups did more poorly.
61. STONE (1981)	253 Ss	Circulatory disorder status, intelligence	Circulatory disorders predicted intellectual functioning in older but not in younger Ss.
62. SZAFRAN (1966)	250 Ss, 50 per decade 20's-60's pilots	Heart rate after exercise, serial choice task	Serial choice task performance was negatively related to heart rate after exercise.

63.	THALER (1956)	52 men, 64 women, over 60 yrs.	EEG, short form Wechsler	Normal/focal EEG related to good short form Wechsler; the opposite was true for diffuse/ mixed EEG.
64.	THOMAS, REILLY (1975)	One 31 year old male runner	Heart rate, lung function, blood glucose, response time	Negative correlaions were found between first two physical variables and response time.
65.	THOMPSON (1975) (replicated: THOMPSON, DAVIS, OBRIST, HEYMAN, 1976)	S = 21, 50-80; Demented with/without vascular involvement; controls	Hyperbaric oxygen treatment, Wechsler Memory Test, Benton Visual Retention Test, Raven, Hooper, Tiens, word using, tapping	No significant relations to oxygen treatment.
66.	THOMPSON, EISDORFER, ESTES (1970)	60-93 yrs. old 432 Ss	Overall cardiovascular disease, by clinical assessment; WAIS, response speed	No siginificant relations were found.
67.	TRIESCHMANN, SAND (1971)	52 men, mean age 39 31 women, mean age 34	Serum creatinine level, WAIS	No significant correlations were found.
68.	WANG (1973)	I 27 Ss, mean age 70 II 24 Ss, age 71-87	I. EEG frequency, WAIS verbal and performance scales; II. cerebral blood flow, WAIS	I. Significant negative relations were found between dominant EEG frequency and the difference between verbal and performance IQ. II. There was only a tendency for positive relations between blood flow and WAIS performance.

69.	WANG, BUSSE (1974)	98 men, 129 women, age means 69.5-73.6	Heart disease status, neurological status, EEG, WAIS	Those with decompensated heart disease had 3 times the theta wave dominance and 3 times the brain disorder rate of those without heart disease. WAIS drop was associated with heart disease over and above that expected by neurological and EEG findings.
70.	WANG, OBRIST, BUSSE (1970)	20 men, 12 women, mean age 69	EEG, WAIS	Slower EEG frequencies were associated with a performance-verbal discrepancy.
71.	WILKIE, EISDORFER (1973)	202 Ss, 60-79 yrs.	WAIS, blood pressure	The first time data were gathered, those in their 70's showed a nonsignificant negative relation between IQ and pressure. The second time, the same was found for those in their 70's; those in their 60's had that nonsignificant effect for performance IQ only.
72.	WILKIE, EISDORFER, NOWLIN (1976)	42 Ss, mean age 67.7	Blood pressure, logical memory, paired associate learning, visual memory	No relation was found between pressure and memory.
73.	WILLIAMS, POTTINGER, SHAPCOTT (1985)	90 men, mean age 20	Arm exercise, choice reaction time, learning	High exercise impaired reaction time; exercise had no effect on learning.

74. WISSLER (1901)	N = 270 men, 47 women undergraduate college students	Massive battery of dozens of physical (e.g., head size, strength) and cognitive (e.g., memory) tests	No relation was found between physical and cognitive tests, or between reaction time and other tests.

Model 2: Physiological Change Over Time Affects Cognitive Change Over the Same Time

1. BARRY, STEINMETZ, PAGE, RODAHL (1966)	7 men, 6 women, avergage 72 yrs.	Physical conditioning, various cognitive measures: tapping, card sort, reaction time, Ravens, short term retention, perception, visual discrimination	Change in physical condition was related to change in ability to produce many words which begin with the same letter.
2. COHEN, SEDLACEK (1983)	15 men, 15 women, age 26-72	Blood pressure, field independence, picture completion, block design, absorption, digit span	Diastolic pressure changes were related to field independence and picture completion.
3. ELIAS, ROBBINS, SHULTZ, STREETEN (1986)	95 Ss (Time 1), 21 Ss (Time 2)	Blood pressure, Halstead-Reitan	No differences were found between normotensives and treated hypertensives.
4. GOLDMAN, KLEINMAN, SNOW, BIDUS, KOROL (1975)	7 male hypertensives and 4 controls, 35-68	Blood pressure, Category Test	As pressure decreased, test scores improved.
5. HAMDY, DAVIES, ARNOLD, TOVEY, SAIMBI, SHORT, EXTON-SMITH (1984)	38 hypertensives, 69-91	Blood pressure, picture matching test	No relation was found between drug-induced pressure changes and performance.
6. JACOBS, WINTER, ALVIS, SMALL (1969)	18 men, mean age 68	Administration of oxygen, Wechsler Memory Scale, Bender-Gestalt, Tien's organic integrity test	Oxygen increased test scores.

7. KLEINMAN, GOLDMAN, SNOW, KOROL (1977)	8 hypertensive men, 26-63	Blood pressure, Category Test	Systolic pressure decrease was negatively related to test improvement.
8. LEDWITH (1970)	92 Ss, age 18-38 (3 women)	Oxygen deprivation, choice reaction time	Oxygen deprivation nonlinearly significantly increased reaction time.
9. MAKSIMOVICH (1983)	60 men, 20-45	Temperature adaptation, memory	(No tests of significance) Adapters improved their memory after ergothermic stress, unlike nonadapters.
10. McGLYNN, LAUGHLIN, RAVE (1979)	15 women, 18-23	Exercise, line matching test	Increase in exercise level was not related to performance on line matching.
11. MILLER, SHAPIRO, KING, GINCHEREAU, HOSUTT (1984)	28 men, 30 women, mean age between 32.1 and 38.3	Blood pressure, 15 psychomotor tests	In hypertensives with behavioral impairment, antihypertensive treatment improved the two-flash threshold, digit symbol test, operative time estimate.
12. POWELL, EISDORFER, BOGDENOFF (1964)	48 men, 20-48 or 60+	Plasma free fatty acid level, word list learning	Older persons had a higher level and continued increase after learning.
13. REITAN, SHIPLEY (1963)	174 men, 25-65	Serum cholesterol, Halstead-Reitan	Reduction of serum cholesterol influenced Halstead scores.

14.	ROBERTSON-TCHABO, ARENBERG, TOBIN, PLOTZ (1986)	52 diabetics and matched controls, 33.0-86.7; 610 additional controls	Diabetes status, WAIS vocabulary, visual memory	No relation was found.
15.	RYMAN, NAITOH, ENGLUND (1985)	100 men, mean age 21.2	Exercise, sentence comprehension	No relation was found.
16.	SCHNEIDER (1983)	2 men, 22 yrs. and 23 yrs.	Blood pressure, attention	Experimentally induced pressure changes of any sor were related to a positive change in attention during sleep.
17.	SHVARTZ, MEROZ, MECHTINGER, BIRNELD (1976)	6 men	Exercise and heat exposure, reaction time	Change from exercise Time 1 to nonexercise Time 2 related to drop in reaction time from Time 1 to Time 2.
18.	THOMAS, REILLY (1975)	1 male runner, age 31	Heart rate, lung function blood glucose, response time	Negative correlation betwee response time and heart rate, vital capacity, forced expiratory volume.
19.	THOMPSON, EISDORFER, ESTES (1970)	250 Ss, 60-93	Cardiovascular status, WAIS, response speed	Relations were not significant.
20.	TOON, BERGEL, JOHNSTON (1984)	12 men, 10 women, mean age 22.5	Blood pressure, reaction time	Experimental manipulation had no effect.
21.	WANG (1973)	27 Ss, mean age 70	EEG, WAIS verbal and performance scales	No relation was found.
22.	WILKIE, EISDORFER (1971)	202 Ss, age 60-79	WAIS, diastolic pressure	Pressure increase was related to performance IQ decrease.

Model 3: Physiological Level at Time One Relates to Change from Time One to Time Two

1. DAVEY (1974)	15 men, 15 women, 17-20	Bicycle ergometer, short term memory (Brown & Poulton Test of Attention)	Higher level of exercise improves performance from Time one to Time two. (Not clearly this model, as exercise continues over time period.)
2. DRUMMOND (1983)	18 hypertensives 18 normotensives mean age 25, 3 women and 15 men in each group	Mental arithmetic, blood pressure	Hypertensives get hyperreactive during testing. (Not clearly this model.)
3. HERZOG, SCHAIE, GRIBBON (1978)	156 Ss (men and women)	Cardiovascular disease diagnosis, intellectual ability (PMA), psychomotor speed (TBR)	CVD group had greater decline over 7 years in intellectual ability and psychomotor speed.
4. SCHULTZ, ELIAS, ROBBINS (1983)	68 male & female hypertensives, ages 45-65 or 21-39, plus 42 normals	Blood pressure, WAIS	Hypertensives' performance deteriorates over 6 years while normotensive's performance improves.
5. SCHULTZ, ELIAS, ROBBINS, STREETEN, BLAKEMAN (1986)	30 hypertensives 24 normotensives	Blood pressure, WAIS	Normotensives improve over time on WAIS verbal scale.
6. SIEGLER (1983)	32 Ss with balanced sexes, 51-77	Cardiovascular disease diagnosis, WAIS	First time CVD not related to WAIS change Time 1 to Time 2.

7. WANG (1973) and WANG, OBRIST, BUSSE (1970)	24-32 Ss, men and women, age 60+	EEG, WAIS, cerebral blood flow	Slower EEG at Time 1 related to greater decline in WAIS performance scale. Focal EEG disturbances at Time one were related to greater drop in verbal IQ Time 1 to Time 2. Low level of blood flow at Time 2 was related to greater decline in verbal IQ, performance IQ, and total IQ from Time 1 to Time 2.

odel 4: Physiological Change from Time 1 to Time 2 Relates to Level at Time 2

No studies found.

odel 5: Physiological Variable at Some Time Related to Cognitive Variable Later--Lagged Effects

1. COSTA, SHOCK (1980)	350 men, 20-65	Blood pressure, Army Alpha	Progressive impairment with time, Time 1 pressure predicts Time 2 cognitive performance. Replicated, with pressure at Time 3 related to performance at Time 6.
2. HERZOG, SCHAIE, GRIBBIN (1978)	156 Ss (men and women)	Cardiovascular status, PMA Test of Behavioral Rigidity	Greater cognitive test improvement at earlier times for those becoming hypertensive at later times.
3. OHLSSON, SJÖBERG, DORNIC (1975)	24 fit males, 21-38 24 less fit males, 20-28	Bicycle ergometer, multiplication problems, prior fitness	Prior fitness influenced later mental performance.

4. SPIETH (1964)	560 men, 35-59	Blood pressure, cardiovascular status, Trailmaking Test, stimulus matching serial reaction time, Halstead Tactual Performance, digit-symbol substitution, block design	Prior history of arteriosclerosis may have been significantly slower than healthy group on composite speeded measures.
5. WILKIE, EISDORFER, NOWLIN (1976)	42 Ss, age 60-69	Blood pressure, memory for designs	Initial pressure related to Time 3 testing of memory for design.
Model 6: Nonlinear Effects			
1. DAVEY (1974)	15 males, 15 females age 17-20	Bicycle ergometer, memory: odd-even digit sequence	Curvilinear relation between exercise and performance such that performance is best at moderate exercise, second best at rest, and poor at hard exercise.
Model 7: Joint, Complex Effects			
1. POWELL, MILLIGAN, FURCHTGOTT (1980)	21 men, 20-35 23 men, 55-70	Blood pressure, serial learning, reaction time	Old begin more sessions with higher pressures than young, and, unlike young, increase pressure during the test. Having this "pressor" response is associated with task success for old.
2. THOMPSON, NOWLIN (1973)	Several subsamples were used; eg. 11, mean age 20 13, mean age 68	Heart rate, blood pressure, response time	For young Ss large changes in heart rate and blood pressure in interval preparatory to an RT Task are related to performance on the task. For old Ss small changes are related to performance.

3. VAN SCHIJNDEL, DE MEY, NARING (1985)	60 men, mean age = 20.1	Blood pressure, anagram performance	Pulse pressure increases for Ss in heavy task demand condition who did well, decreases for those in light task demand condition who did well.

Studies Related to Terminal Drop*

1. BAER, GAITZ (1971)	100 psychiatric patients age 60+	Battery of physical status measures, battery of cognitive status factors, live/die status	Physical factors predict better than cognitive factors whether S lives or dies.
2. BERKOWITZ (1965)	184 men, average age 65	Wechsler-Bellevue, live/die status	Greater decline was found for those who died.
3. BIRREN (1964)	47 men, over age 65	WAIS live/die status	There was a significant decline in WAIS scores before death, regardless of initial level.
4. BIRREN (1965)	47 men	EEG, WAIS, Raven, live/die status	WAIS and Raven scores distinguished lived from died.
5. BOTWINICK, WEST, STORANDT (1978)	166 Ss, 60-89	Wechsler Memory Scale, Bender-Gestalt, Hooper Visual Organization, digit symbol, crossing off, trailmaking, live/die status	Survivors scored better on the cognitive measures.
6. CUNNINGHAM, HUCHENDORF, WHITE (1984)	1000 men and women (65% women), 51-91	Vocabulary, numerical facility, perceptual speed, live/die status	Change in cognition predicted survival status

*Categorization by model supposes that one can decide conceptually whether "lived/died" is a status level or a change or a lagged effect. Since this is an open question, model category must be supplied by the reader.

7. GOLDFARB (1969)	1280 persons 64+ yrs.; females outnumbered men two to one	Mental status exam, live/die status	Poor mental status scores predicted survival.
8. GRANICK (1971)	47 men, mean age = 71.5, 65-91	Stored information, WAIS subscales, Raven, Mill Hill Vocabulary, reaction time, copy speed, live/die status	Performance on cognitive tests listed here predicted survival.
9. JARVIK, BLUM (1971) and JARVIK, FALEK (1963)	78 men and women, at least 60 yrs.	Vocabulary, similarities, digit symbol substitution, live/die status	Cognitive test peformance predicted survival.
10. KLEEMEIER (1962)	I. 114 men II. 70 men 65-92	I. EEG, live/die status II. Wechsler-Bellevue Performance and Verbal Scales, live/die status	I.&II. EEG Mean change and W-B Performance Scale predicted survival.
11. LIEBERMAN (1965)	25 Ss	Bender Gestalt, live/die status	Change on B-G predicted survival.
12. LIEBERMAN (1971)	180 males & females, mean age 78	Combined scores on cognitive measures such as mental status, learning, visual organization= cognitive functioning; live/die status; stressed/nonstressed status	Cognitive functioning predicted survival in the stressed group.
13. PFEIFFER (1970)	74 men and women, mean age 67	WAIS, live/die status	IQ's of survivors were higher at Time 1 than those of ones who died. WAIS-P was higher for both men and women; WAIS-V for men only.
14. REMAINS, GREEN (1971)	187 men, mean age 68	WAIS, live/die status	There was greater decline in WAIS IQ or subscales for those who died.

15.	RIEGEL (1971) and RIEGEL, (1972)	380 men and women, 55-75	WAIS, verbal achievement tests, live/die status	Drop in scores was related to death.
16.	RIEGEL, RIEGEL, MEYER (1967)	74 men, 190 women, 264 longitudinal study drop outs, 62 of whom died, 55 and older, average age = 79.0	WAIS, verbal ability tests, live/die status	Survival was not related to cognition.
17.	TRIESCHMANN, SAND (1971)	83 men and women, average age 34 (women) and 39 (men)	WAIS subscale, live/die status	Survival status was related to WAIS subscales.
18.	WILKIE, EISDORFER (1974)	256 Ss, men and women, mean ages = 74, 77, and 80	WAIS full scale score, live/die status	No relation between WAIS level scores and survival; those who died showed significant changes 13-32 months prior to death.

Table 2

Summary of Significant MR Analyses for Model 7, Relating Age, Blood Pressure and BVRT Errors

Dependent Variable (level/change, ordered by time)	Independent Variables (age, diastolic/systolic pressures) (level/change, ed by time) (transformed variables are indicated by the variable numbers preceded by "D")	B	MR	R^2 change
Diastolic, All Clean Group(N = 142)				
BVRT change T1-T2	Age	.03	.15	.02
	D10 #positive D changes to T2	2.93	.25	.04
BVRT Time 2	Age	.13	.53	.28
	D16 #very negative D changes to T2	-2.59	.55	.02
BVRT Time 3	Age	.18	.58	.34
	D16 #very negative D changes to T2	-3.22	.60	.02
BVRT Time 2	Age	.12	.53	.28
	D10 #positive D changes to T2	2.49	.56	.03

BVRT change T1-T2	Age	.03	.15	.02
	D12	-2.61	.24	.04
	#negative D changes to T2			
Systolic, All Clean Group (N = 151)				
BVRT change T2-T3	Age	.06	.22	.05
	D13	-4.08	.33	.06
	#very positive S changes to T2			
BVRT change T2-T3	Age	.06	.22	.05
	D17	-.12	.31	.04
	$\bar{X}$ S change positive changes weighted to T2			
BVRT change T2-T3	Age	.05	.22	.05
	D27	-.10	.31	.04
	$\bar{X}$ S changes from T2-3			
BVRT change T2-T3	Age	.06	.22	.05
	D33	-2.52	.31	.04
	#positive S changes from T2-3			
BVRT change T2-T3	Age	.05	.22	.05
	D47	-.05	.27	.02
	$\bar{X}$ S change negative changes weighted, from T2-3			

Diastolic, Old Group (N = 51)				
BVRT Time 2	Age	.38	.37	.13
	D8 Root $\bar{X}$ square D change to T2	-.33	.46	.08
BVRT Time 3	Age	.20	.19	.03
	D26 Highest D change from T2-3	-.20	.34	.09
BVRT change T1-T2	Age	.31	.32	.10
	D2 Highest D change to T2	-.17	.40	.06
Systolic, Old Group (N = 55)				
BVRT Time 3	Age	.23	.19	.03
	D25 Highest S change from T2-3	-.10	.34	.09
BVRT Time 3	Age	.23	.19	.03
	D27 $\bar{X}$ S change from T2-3	-.24	.36	.10
BVRT Time 3	Age	.18	.19	.03
	D33 #positive S changes from T2-3	-11.29	.48	.20

BVRT Time 3	Age	.22	.19	.03
	D45	-.13	.36	.09
	$\bar{X}$ change, positive S change weighted, from T2-3			
BVRT Time 3	Age	.17	.19	.03
	D35	9.04	.38	.12
	#negative S changes from T2-3			
BVRT Time 3	Age	.13	.19	.03
	D57	-14.39	.36	.10
	#positive S changes to T3			
BVRT change T1-T3	Age	.21	.16	.02
	D11	-7.90	.42	.15
	#negative S changes to T2			
Diastolic, Old Clean Group (N = 28)				
BVRT Time 3	Age	.01	.07	.00
	D14	-13.84	.38	.15
	#very positive D changes to T2			
Systolic, Old Clean Group (N = 33)				
BVRT Time 3	Age	-.06	.08	.00
	D51	-1.23	.47	.22
	$\bar{X}$ S change to T3			

BVRT Time 3	Age	-.08	.08	.00
	D57	-19.74	.43	.18
	#positive S changes to T3			
BVRT Change T2-T3	Age	.02	.14	.01
	D27	-.26	.40	.15
	$\bar{X}$ S change from T2-3			
BVRT Change T2-T3	Age	.02	.14	.01
	D33	-7.63	.42	.17
	#positive S changes from T2-3			
BVRT Change T1-T3	Age	.17	.07	.00
	D3	.43	.37	.14
	$\bar{X}$ S changes to T2			
BVRT Change T1-T3	Age	.15	.07	.00
	D11	-8.71	.39	.15
	#negative S changes to T2			
BVRT Change T1-T3	Age	.23	.07	.00
	D23	.35	.41	.17
	$\bar{X}$ very negative S changes to T2			
BVRT Change T1-T3	Age	.07	.07	.00
	D51	-.98	.37	.14
	$\bar{X}$ S change to T3			

Diastolic, Young Group (N = 55)				
BVRT Change T1-T2	Age	.11	.23	.05
	D2	.10	.35	.07
	Highest D change to T2			
BVRT Change T1-T3	Age	-.02	.00	.00
	D2	.10	.28	.08
	Highest D change to T2			
Systolic, Young Group (N = 59)				
BVRT Time 3	Age	.04	.09	.00
	D47	-.08	.27	.07
	$\overline{X}$ negative S change weighted, from T2-3			
BVRT Change T2-T3	Age	-.13	.27	.07
	D19	.11	.36	.06
	$\overline{X}$ negative S change weighted, to T2			
BVRT Change T1-T3	Age	.02	.00	.00
	D59	4.50	.28	.08
	#negative S changes to T3			
BVRT Change T2-T3	Age	-.13	.27	.07
	D15	-2.94	.38	.07
	#very negative S changes to T2			

BVRT Change T1-T2	Age	.13	.22	.05
	D15	4.03	.37	.08
	#very negative S changes to T2			
Diastolic, Young Clean Group (N = 32)				
BVRT Time 2	Age	.12	.25	.06
	D8	-.28	.47	.22
	Root of $\bar{X}$ squared D change to T2			
BVRT Change T2-T3	Age	-.11	.21	.04
	D8	.29	.43	.14
	Root of $\bar{X}$ squared D change to T2			
BVRT Change T2-T3	Age	-.11	.21	.04
	D16	5.39	.46	.17
	#very negative D changes to T2			
BVRT Time 2	Age	.12	.25	.06
	D16	-5.13	.49	.18
	#very negative D changes to T2			
Systolic, Young Clean Group (N = 35)				
BVRT Change T2-T3	Age	-.05	.20	.04
	D17	-.22	.39	.11
	$\bar{X}$ S positive change weighted, to T2			

Table 3

Summary of Significant MR Analyses Relating Age, Blood Pressure and WAIS-V, by Model

	Dependent Variable (level/change, ordered by time)	Independent Variables (Age, D or S pressure) (level/change, ordered by time)[Delta (transformed) variables indicated by "Dn"]	B	MR	R^2 change
Model 1					
	WAIS-V Time 1	Age	.201	.11	.01
	(All Ss, N=129)	Systolic Time 1	-.199	.19	.02
		Diastolic Time 1	.224	.25	.04
Model 6	(N=290) (All Ss)				
	WAIS-V Time 3	Age	-.04	.03	.00
		D10	-5.13	.12	.01
		# positive D changes to T2			
	WAIS-V Time 3	Age	-.03	.03	.00
		D8	.29	.14	.01
		$\bar{X}$ D change from T2-3			
	WAIS-V Time 3	Age	-.03	.03	.00
		D40	-5.64	.11	.01
		# drops D from T2-3			
	WAIS-V Time 3	Age	-.02	.03	.00
		D36	-4.31	.13	.01
		# drops D from T2-3			
	WAIS-V Time 3	Age	-.03	.03	.00
		D48	.21	.15	.02
		$\bar{X}$ very negative D change from T2-3			

Model 6 (cont'd.)

WAIS-V Time 3	Age	-.03	.03	.00
	D44	.34	.12	.01
	$\bar{X}$ very negative D change from T2-3			
WAIS-V Time 3	Age	-.03	.03	.00
	D35	-5.38	.14	.02
	$\bar{X}$ negative S change from T2-3			
WAIS-V Change 2-3	Age	-.02	.11	.01
	D25	-.05	.18	.02
	Highest change S from T2-3			
WAIS-V Change 2-3	Age	-.03	.11	.01
	D31	-.08	.17	.01
	Root $\bar{X}$ sq. S change from T2-3			
WAIS-V Change 2-3	Age	-.03	.11	.01
	D37	-3.74	.17	.02
	# very positive S changes from T2-3			
WAIS-V Change 2-3	Age	-.03	.11	.01
	D41	-.13	.19	.02
	$\bar{X}$ S change weighted for high, from T2-3			
WAIS-V Change 2-3	Age	-.04	.11	.01
	D64	-4.34	.16	.01
	# low D changes to T3			
WAIS-V Change 2-3	Age	-.04	.11	.01
	D68	.30	.17	.01
	$\bar{X}$ D changes very low weighted to T3			

				Models
				77
WAIS-V Change 1-3	Age	-.11	.27	.07
	D64	-6.17	.31	.02
	# low D changes to T3			
WAIS-V Change 1-3	Age	-.11	.27	.07
	(D68)	.39	.31	.02
	$\bar{X}$ D change weighted low to T3			
WAIS-V Change 1-3	Age	-.11	.27	.07
	(D72)	.17	.30	.02
	$\bar{X}$ D change weighted low to T3			

Model 7

Linear Relations

(N)					
34(YC)	WAIS-V Time 3	Age	-.06	.03	.00
		Systolic Time 3	-.36	.40	.16
32(YC)	WAIS-V Time 3	Age	-.26	.03	.00
		Diastolic Time 3	-.52	.47	.22
28(Old)	WAIS-V Change 1-3	Age	-.11	.03	.00
		Systolic change 1-3	.08	.42	.17
17(OC)	WAIS-V Change 1-3	Age	-.26	.00	.00
		Systolic change 1-3	.13	.60	.36
70(AC)	WAIS-V Time 3	Age	-.05	.01	.00
		Systolic change 1-3	.13	.32	.10
11(YC)	WAIS-V Time 3	Age	-1.19	.02	.00
		Systolic change 1-2	.72	.73	.53

				Models	
					78
32(YC)	WAIS-V Time 3	Age	.00	.02	.00
		Systolic change 2-3	-.36	.37	.13
31 (Old)	WAIS-V Time 3	Age	.42	.09	.00
		Systolic change 1-2	-.27	.20	.04
		Diastolic change 1-2	.49	.45	.16
32(YC)	WAIS-V Time 3	Age	.05	.03	.00
		Diastolic Time 1	-.56	.39	.15

Nonlinear Relations

Diastolic, All Clean Group (N=158)

WAIS-V Time 3	Age	-.00	.01	.01
	D4	-.54	.17	.03
	$\bar{X}$ change to T2			
WAIS-V Time 3	Age	—	.01	.00
	D10	-7.42	.16	.02
	# positive changes to T2			
WAIS-V Time 3	Age	-.00	.01	.00
	D24	-.35	.17	.03
	$\bar{X}$ change, negatives weighted, to T2			
WAIS-V Time 3	Age	.00	.01	.00
	D58	-11.06	.16	.02
	# positive changes to T3			
WAIS-V Change T2-T3	Age	-.03	.12	.01
	D64	-6.64	.21	.03
	# very negative changes to T3			

WAIS-V Change T1-T3	Age	-.13	.32	.10
	D64	-6.62	.35	.02
	# very negative changes to T3			

Systolic, All Clean Group (N=158)

WAIS-V Change T1-T2	Age	-.09	.22	.04
	D11	-3.33	.27	.03
	# negative changes to T2			
WAIS-V Change T2-T3	Age	-.02	.12	.01
	D25	-.06	.21	.03
	Highest change from T2-3			
WAIS-V Change T2-T3	Age	-.03	.12	.01
	D29	-.00	.20	.03
	$\bar{X}$ squared change from T2-3			
WAIS-V Change T2-T3	Age	-.02	.12	.01
	D31	-.11	.21	.03
	Root of squared change from T2-3			
WAIS-V Change T2-T3	Age	-.03	.12	.01
	D37	-5.72	.22	.04
	# very positive changes from T2-3			
WAIS-V Change T2-T3	Age	-.03	.12	.01
	D41	-.18	.22	.04
	$\bar{X}$ changes positives weighted from T2-3			
WAIS-V Change T2-T3	Age	-.02	.12	.01
	D49	-.06	.19	.02
	Highest change to T3			

			Models	
				80
WAIS-V Change T2-T3	Age	-.02	.12	.01
	D55	-.13	.19	.02
	Root squared change to T3			
WAIS-V Change T1-T3	Age	-.14	.32	.10
	D11	-3.13	.35	.02
	# negative changes to T2			
Diastolic, Old Group (N=62)				
WAIS-V Time 3	Age	.22	.09	.00
	D26	.51	.34	.11
	Highest change from T2-3			
WAIS-V Time 3	Age	.20	.09	.00
	D44	1.04	.26	.07
	$\bar{X}$ change very negative changes weighted, from T2-3			
WAIS-V Time 3	Age	.15	.09	.00
	D28	1.17	.38	.14
	$\bar{X}$ change from T2-3			
WAIS-V Time 3	Age	.17	.09	.00
	D46	.60	.32	.10
	$\bar{X}$ change very positive changes weighted, from T2-3			
WAIS-V Time 3	Age	.17	.09	.00
	D48	.81	.39	.15
	$\bar{X}$ change very negative change weighted, from T2-3			
WAIS-V Time 3	Age	.17	.09	.00
	D36	-18.48	.36	.13
	# negative changes from T2-3			

			Models	
				81
WAIS-V Change T2-T3	Age	.02	.00	.00
	D6	-.01	.27	.07
	$\bar{X}$ squared change to T2			
WAIS-V Change T2-T3	Age	.03	.00	.00
	D8	-.32	.29	.08
	Root squared change to T2			
WAIS-V Change T1-T3	Age	.01	.03	.00
	D2	-.24	.29	.08
	Highest change to T2			
WAIS-V Change T1-T3	Age	-.02	.03	.00
	D18	-.60	.26	.07
	$\bar{X}$ change very positive weighted, to T2			
WAIS-V Change T1-T3	Age	-.03	.03	.00
	D58	11.60	.29	.08
	# positive changes to T3			
Systolic, Old Group (N=62)				
WAIS-V Time 3	Age	.23	.09	.00
	D33	14.68	.28	.08
	# positive changes from T2-3			
WAIS-V Change T2-T3	Age	-.00	.00	.00
	D33	4.79	.24	.06
	# positive changes from T2-3			
WAIS-V Change T2-T3	Age	.02	.00	.00
	D57	9.79	.27	.07
	# positive changes to T3			

			Models	
				82
WAIS-V Change T1-T3	Age	-.00	.03	.00
	D71	.31	.25	.06
	$\bar{X}$ change very negative weighted, to T3			
Diastolic, Old Clean Group (N=37)				
WAIS-V Change T1-T3	Age	.12	.00	.00
	D2	-.38	.45	.20
	Highest change to T2			
WAIS-V Change T1-T3	Age	.02	.00	.00
	D18	-.81	.36	.13
	$\bar{X}$ change very positive changes weighted, to T2			
WAIS-V Change T1-T3	Age	.03	.00	.00
	D22	-.51	.39	.15
	$\bar{X}$ change very positive changes weighted, to T2			
Systolic, Old Clean Group (N=37)				
WAIS-V Change T1-T2	Age	.17	.15	.02
	D1	-.10	.34	.10
	Highest change to T2			
WAIS-V Change T1-T2	Age	.16	.15	.02
	D7	-.19	.37	.12
	Root squared changes to T2			
WAIS-V Change T1-T2	Age	.19	.15	.02
	D15	-10.97	.40	.14
	# very negative changes to T2			
WAIS-V Change T1-T2	Age	.18	.15	.02

	D19	.39	.37	.11
	$\bar{X}$ change very negative changes weighted, to T2			
WAIS-V Change T2-T3	Age	-.36	.15	.02
	D33	13.92	.62	.37
	# positive changes from T2-3			
WAIS-V Change T2-T3	Age	-.16	.15	.02
	D57	21.93	.54	.27
	# positive changes to T3			
WAIS-V Change T2-T3	Age	-.23	.15	.02
	D35	-10.29	.42	.15
	# negative changes from T2-3			
WAIS-V Change T1-T3	Age	.02	.00	.00
	D65	-.45	.31	.10
	$\bar{X}$ change very positive changes weighted, to T3			
WAIS-V Change T1-T3	Age	.02	.00	.00
	D7	-.20	.32	.10
	Root squared change to T2			
WAIS-V Change T1-T3	Age	.03	.00	.00
	D55	-.24	.32	.10
	Root squared change to T3			
WAIS-V Change T1-T3	Age	.02	.00	.00
	D67	.56	.32	.10
	$\bar{X}$ change very negative changes weighted, to T3			
WAIS-V Change T1-T3	Age	.01	.00	.00
	D71	.58	.38	.14
	$\bar{X}$ change very negative changes weighted, to T3			

Diastolic, Young Group ----------

Systolic, Young Group (N=61)

WAIS-V Time 3	Age	-.27	.07	.00
	D31	-.45	.26	.07
	Root squared change from T2-3			

Diastolic, Young Clean Group (N=34)

WAIS-V Time 3	Age	-.39	.03	.00
	D10	-17.65	.34	.12
	# positive changes to T2			
WAIS-V Time 3	Age	-.43	.03	.00
	D52	-3.01	.44	.19
	$\bar{X}$ change to T3			
WAIS-V Time 3	Age	-.22	.03	.00
	D72	-1.52	.36	.13
	$\bar{X}$ very negative change weighted, to T3			
WAIS-V Change T1-T2	Age	-.24	.22	.05
	D2	.37	.42	.13
	Highest change to T2			
WAIS-V Change T1-T2	Age	-.14	.22	.05
	D12	-8.29	.39	.10
	# negative changes to T2			

Systolic, Young Clean Group (N=34)

WAIS-V Time 3	Age	-.05	.03	.00
	D27	-.71	.33	.11
	$\bar{X}$ change from T2-3			

				Models
				85
WAIS-V Time 3	Age	-.00	.03	.00
	D33	-17.37	.41	.17
	# positive changes from T2-3			
WAIS-V Time 3	Age	-.10	.03	.00
	D45	-.61	.35	.12
	$\bar{X}$ change very positive change weighted, from T2-3			
WAIS-V Time 3	Age	-.00	.03	.00
	D57	-27.32	.36	.13
	# positive changes to T3			